

REMARKS

This application is amended in a manner believed to place it in condition for allowance at the time of the next Official Action.

The claims 1, 2, 4, 6-10, 13 are amended. Support for the amendment to claims may be found, for example at specification page 2, line 3-13.

Claims 1-4, 6-10 and 13 are pending.

Claims 3, 6-8, and 10 are withdrawn as being drawn to non-elected species.

Also included with this amendment is a corrected Declaration Under Rule 132 as filed May 3, 3007. Table 2 of the previously filed declaration did not include statistics.

Claims 1, 2, 4, 9 and 13 stand rejected under 35 USC 103(a) as being unpatentable over the combination of DI PIERRO WO 02/098436 ("DI PIERRO") and ZNAIDEN et al. US 5,523, 090 ("ZNAIDEN"). This rejection is respectfully traversed.

The position maintained by Official Action is that DI PIERRO discloses a composition for the treatment of cellulite, which comprises 0.1-2.5% complex of escin/beta-siterol with phospholipids and 0.1-2.5% *Ginkgo biloba* dimeric flavononoids with phospholipids. The Official Action acknowledges that DI PIERRO does not teach the incorporation of the claimed first vasoactive agent visnadin into a composition.

ZNAIDEN is offered for teaching an anti-cellulite composition comprising *Ginkgo biloba* extract and escin. The Official Action further states that suitable vasoactive compounds include, but are not limited to visnadin.

The position of the Official Action is that it would have obvious to one of ordinary skill in the art to combine the ingredients of DI PIERRO and ZNAIDEN because both teach compositions for treating cellulite.

However, the proposed combination cannot render obvious the claimed invention for at least three reasons:

I. The combination does not teach the claimed invention.

The present are amended so as to recite that the combination of vasoactive compounds "consists of" the three vasoactive agents recited. That is, the claimed compositions do not include vasoactive compound other than those included in the claimed vasoactive agents.

DI PIERRO requires at least a combination 4 vasoactive ingredients (plus one optional):

- a) complex of escin/beta-sitosterol with phospholipids.
- b) complex of *Ginkgo biloba* dimeric flavonoids with phospholipids,
- c) complex of *Centella asiatica* triterpenes with phospholipids,

and optionally one or both of:

- d) ethylximeninate, and
- e) standardized *Coleus forskollii* extract.

DI PIERRO fails to disclose or suggest that any one component or combination of less than four is capable of producing the same effect.

ZNAIDEN teaches a skin treatment composition containing an alpha hydroxy acid and/or an inositol phosphoric acid in combination with a xanthine. Visnadin is indicated as one of the many optional ingredients that may be present in the cosmetic composition. See, e.g., column 6, lines 54-55 and column 7, line 13.

Thus, even if one would have been motivated to arbitrarily add a merely "optional" ingredient with unknown activity, at best, the combination would include more than the vasoactive agents included in the claimed combination.

II. There would be no expectation of success in forming the claimed composition.

DI PIERRO requires at least four agents to be effective. DI PIERRRO fails to disclose or suggest that the *Gingko biloba* dimeric flavones complexed with phospholipids and escin beta-sitosterol complexed with phospholipids, alone, would be an effective pairing of the vasoactive agents. Indeed, based

on the teachings of DI PIERRO, one would have expected inferior results with less than the required four agents.

ZNAIDEN discloses visnadin as one of many optional ingredients that may be present in a cosmetic composition that reduces signs of cellulite. That is, ZNAIDEN appears to suggest that such optional ingredients do not provide the desired anti-cellulite effect. See, e.g., column 6, lines 54-55 and column 7, line 13. Accordingly, one of ordinary skill in art faced with the problem of finding an effective anti-cellulite composition alternative to that disclosed in ZNAIDEN would not have seriously contemplated using visnadin, which is identified as an optional component that is not essential for obtaining the anti-cellulite effect.

Thus, there would not have been any expectation of success in arbitrarily combining two active ingredients from DI PIERRO and an option ingredient from ZNAIDEN.

III. There is no recognition of the synergistic anti-cellulite effect of the claimed combination of vasoactive agents.

There is no suggestion that a combination of only two of the vasoactive components of DI PIERRO and an optional ingredient of unknown efficacy from ZNAIDEN would have any type of synergistic anti-cellulite effect. There is not even a recognition of these vasoactive components of DI PIERRO being preferred.

Unexpected results observed by claimed combination were filed in the Rule 132 Declaration of May 30, 2007. The Official Action, however, states that "there is no significant difference between the before and after treatment data". Accordingly, a new Rule 132 Declaration is provided in the Appendix of this amendment that provides the statistics for Table 2, which were erroneously omitted in the previously filed declaration. Thus, the data does show a significant difference.

The Official Action also states that the declaration should compare the composition of vasoactive ingredients from DI PIERRO with and without the optional ingredient of ZNAIDEN.

However, the purpose of the declaration is to show that there is an unexpected synergistic result achieved by the claimed composition. Accordingly, the individual components and the combination are evaluated for their efficacy to demonstrate that the efficacy of the combination of components is greater than the efficacy predicted by the combination of the efficacy of the individual components.

As explained previously, the declaration compares a gel formulation of the claimed invention comprising the three vasoactive agents to three gel formulations including a single active ingredient, and a single placebo formulation. Each of the gel formulations includes the same excipient base.

The gel formulations are compared for their ability to reduce cellulite in Tables 1 and 2 (e.g. in terms of thigh

macrorelief (Rz) and thigh circumference (cm)). The tables demonstrate that the claimed invention (group 5) proved more effective in reducing thigh macrorelief and thigh circumference than the formulations based on these ingredients individually (groups 2, 3, and 4), and that there is a significant statistical difference before and after treatment.

Tables 1 and 2 further demonstrate that there is a significant statistical difference between thigh macrorelief (Rz) and thigh circumference (cm)). The three active ingredients behave synergistically, as the effect of three components together is greater than the sum of the effects of each single component.

The cited publication neither suggest the combination of the claimed active ingredients nor a synergistic effect would result from the combination of claimed active ingredients.

Therefore, the proposed combination fails to render obvious the claimed invention for at least the three reasons discussed above, and withdrawal of the rejection is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



---

Robert Madsen, Reg. No. 58,543  
209 Madison Street, Suite 500  
Alexandria, VA 22314  
Telephone (703) 521-2297  
Telefax (703) 685-0573  
(703) 979-4709

RAM/jr

**APPENDIX:**

The Appendix includes the following item:

-Declaration under Rule 132